

**ABSTRACT OF THE DISCLOSURE**

Disclosed are viral variants exhibiting reduced sensitivity to particular agents including nucleoside analogues and immunological mediators such as immunoglobulins and immune  
5 cells. Also provided are hepatitis B virus (HBV) variants which exhibit a level of replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of the nucleoside analogue. The present invention also provides methods of treating HBV infection, including a method for identifying a need to change or otherwise alter an existing therapeutic regimen. Also disclosed are methods for monitoring the development in a subject of an  
10 increased HBV load in the presence of a nucleoside analogue. The present invention further provides the use of nucleoside analogue-resistant HBV variants which exhibit a similar or increased replication fitness in the presence of the nucleoside analogue compared to in the absence of the nucleoside analogue to screen for medicaments to treat HBV infection.

0987740-060301